

2 We claim:

- 3 1. A device for fluid mixing and gas exchange comprising:  
4 a housing defining a chamber for holding a liquid, wherein at least 1 wall of  
5 the chamber comprises a plurality of gas-permeable portions, and wherein the gas-  
6 permeable portions are selectively deflectable into the interior of the chamber.
- 7 2. The device of claim 1, wherein 1 wall comprises a plurality of gas-permeable  
8 portions.
- 9 3. The device of claim 1, wherein 2 walls comprise a plurality of gas-permeable  
10 portions.
- 11 4. The device of claim 1, wherein at least 2 walls comprise a plurality of gas-permeable  
12 portions.
- 13 5. The device of claim 1, wherein at least one wall of the chamber comprises at least 3  
14 selectively deflectable gas-permeable portions.
- 15 6. The device of claim 1, wherein at least one wall of the chamber comprises at least 4  
16 selectively deflectable gas-permeable portions.
- 17 7. The device of claim 1, wherein at least one wall of the chamber comprises at least 5  
18 selectively deflectable gas-permeable portions.
- 19 8. The device of claim 1, wherein at least one wall of the chamber comprises at least 6  
20 selectively deflectable gas-permeable portions.
- 21 9. The device of claim 1, wherein at least one wall of the chamber comprises between 6  
22 and 10 selectively deflectable gas-permeable portions
- 23 10. The device of claim 1, wherein at least one wall of the chamber comprises at least 10  
24 selectively deflectable gas-permeable portions.
- 25 11. The device of claim 1, wherein the total area of the selectively deflectable portions is  
26 at least 25% of the area of the wall that comprises them.

- 1 12. The device of claim 1, wherein the total area of the selectively deflectable portions is  
2 at least 50% of the area of the wall that comprises them.
- 3 13. The device of claim 1, wherein the total area of the selectively deflectable portions is  
4 at least 75% of the area of the wall that comprises them.
- 5 14. The device of claim 1, wherein the selectively deflectable portions are spaced apart.
- 6 15. The device of claim 1, wherein the selectively deflectable portions are separated by  
7 non-deflectable portions of the wall.
- 8 16. The device of claim 1, wherein the selectively deflectable portions are substantially  
9 parallel to one another.
- 10 17. The device of claim 1, wherein the selectively deflectable portions have uniform  
11 widths in the plane of the wall that comprises them.
- 12 18. The device of claim 1, wherein at least one selectively deflectable portion has a  
13 nonuniform width in the plane of the wall that comprises the selectively deflectable  
14 portion.
- 15 19. The device of claim 18, wherein adjacent deflectable portions comprise  
16 complementary convex and concave regions.
- 17 20. The device of claim 1, wherein the volume of the chamber is at least 0.5  $\mu\text{l}$ .
- 18 21. The device of claim 1, wherein the volume of the chamber is between 0.5  $\mu\text{l}$  and 10  
19  $\mu\text{l}$ .
- 20 22. The device of claim 1, wherein the volume of the chamber is between 10  $\mu\text{l}$  and 50  
21  $\mu\text{l}$ .
- 22 23. The device of claim 1, wherein the volume of the chamber is between 50  $\mu\text{l}$  and 150  
23  $\mu\text{l}$ .
- 24 24. The device of claim 1, wherein the volume of the chamber is between 150  $\mu\text{l}$  and  
25 500  $\mu\text{l}$ .

- 1 25. The device of claim 1, wherein the volume of the chamber is between 500  $\mu$ l and 1  
2 ml.
- 3 26. The device of claim 1, wherein the chamber is macroscopic.
- 4 27. The device of claim 1, wherein the ratio of the area of the wall of the chamber  
5 comprising deflectable portions to the volume of the chamber is at least 50/m.
- 6 28. The device of claim 1, wherein the ratio of the area of the wall of the chamber  
7 comprising deflectable portions to the volume of the chamber is between 50/m and  
8 20,000/m.
- 9 29. The device of claim 1, wherein the ratio of the area of the wall of the chamber  
10 comprising deflectable portions to the volume of the chamber is between 100/m and  
11 10,000/m.
- 12 30. The device of claim 1, wherein a deflectable portion is constrained so that it does not  
13 move along its perimeter when actuated.
- 14 31. The device of claim 1, wherein the deflectable portions are independently  
15 deflectable.
- 16 32. The device of claim 1, wherein at least some of the deflectable portions are not  
17 independently deflectable.
- 18 33. The device of claim 1, wherein at least some of the deflectable portions are  
19 deflectable in groups.
- 20 34. The device of claim 33, wherein the deflectable portions in a group deflect at the  
21 same time.
- 22 35. The device of claim 33, wherein the deflectable portions in a group deflect at  
23 different times.
- 24 36. The device of claim 1, wherein the deflectable portions form part of a continuous  
25 gas-permeable layer of material.

- 1 37. The device of claim 1, wherein the thickness of the deflectable portions is between 1-  
2 1000  $\mu\text{m}$ .
- 3 38. The device of claim 1, wherein the thickness of the deflectable portions is between 5-  
4 500  $\mu\text{m}$ .
- 5 39. The device of claim 1, wherein the thickness of the deflectable portions is between  
6 and 100-300  $\mu\text{m}$ .
- 7 40. The device of claim 1, wherein the gas-permeable deflectable portions are  
8 deflectable at a rate between 1 – 1,000 Hz.
- 9 41. The device of claim 1, wherein the gas-permeable deflectable portions are  
10 deflectable at a rate between 10 - 500 Hz.
- 11 42. The device of claim 1, wherein the gas-permeable deflectable portions are  
12 deflectable at a rate between 25 – 200 Hz.
- 13 43. The device of claim 1, wherein the gas-permeable deflectable portions are permeable  
14 to oxygen.
- 15 44. The device of claim 1, wherein the gas-permeable deflectable portions have a  
16 diffusivity for  $\text{O}_2$  greater than  $1.0 \times 10^{-5} \text{ cm}^2/\text{s}$ .
- 17 45. The device of claim 1, wherein the gas-permeable deflectable portions have a  
18 diffusivity for  $\text{O}_2$  greater than  $2.0 \times 10^{-5} \text{ cm}^2/\text{s}$ .
- 19 46. The device of claim 1, wherein the gas-permeable deflectable portions have a  
20 diffusivity for  $\text{O}_2$  greater than  $3.0 \times 10^{-5} \text{ cm}^2/\text{s}$ .
- 21 47. The device of claim 1, wherein the gas-permeable deflectable portions are made of a  
22 material in which the solubility of  $\text{O}_2$  is greater than  $5 \times 10^{-3} \text{ mol/Liter}$  for air at 1  
23 atm.
- 24 48. The device of claim 1, wherein the gas-permeable deflectable portions are made of a  
25 material in which the solubility of  $\text{O}_2$  is greater than  $1.0 \times 10^{-3} \text{ mol/Liter}$  for air at 1  
26 atm.

- 1 49. The device of claim 1, wherein the gas-permeable deflectable portions have a  
2 permeability to O<sub>2</sub> of between 750 and 850 Barrer.
- 3 50. The device of claim 1, wherein the gas-permeable deflectable portions have a  
4 permeability to O<sub>2</sub> of between 850 and 1000 Barrer.
- 5 51. The device of claim 1, wherein the gas-permeable deflectable portions have a  
6 permeability to O<sub>2</sub> of between 400 and 750 Barrer.
- 7 52. The device of claim 1, wherein the gas-permeable deflectable portions have a  
8 permeability to O<sub>2</sub> of less than 400 Barrer.
- 9 53. The device of claim 1, wherein the gas-permeable deflectable portions are permeable  
10 to CO<sub>2</sub>.
- 11 54. The device of claim 1, wherein the deflectable portions comprise an elastomeric  
12 material.
- 13 55. The device of claim 54, wherein the elastomeric material is PDMS.
- 14 56. The device of claims 1, 36, or 54 wherein the housing and the deflectable portions  
15 comprise different materials.
- 16 57. The device of claims 1, 36, or 54, wherein the housing and the deflectable portions  
17 comprise the same material.
- 18 58. The device of claims 1, 36, or 54, wherein the housing and the deflectable portions  
19 comprise an elastomeric material.
- 20 59. The device of claim 58, wherein the elastomeric material is PDMS.
- 21 60. The device of claim 1, wherein at least a portion of the housing is made of a material  
22 selected from the group consisting of: glass, plastic, or metal.
- 23 61. The device of claim 1, further comprising a substrate, wherein the housing is  
24 positioned on the substrate.
- 25 62. The device of claim 61, wherein the substrate forms a wall of the chamber.

- 1 63. The device of claim 1, each portion is deflectable by pressurizing a cavity in  
2 communication with the deflectable portion or by pressurizing a cavity in  
3 communication with a different deflectable portion.
- 4 64. The device of claim 1, wherein at least one deflectable portion is deflectable by  
5 pressurizing a cavity in communication with a different deflectable portion.
- 6 65. The device of claim 1, wherein each deflectable portion is in communication with a  
7 cavity.
- 8 66. The device of claim 65, wherein the cavities are not connected with one another.
- 9 67. The device of claim 63, wherein at least two of the cavities are connected with one  
10 another via a hollow region that has a substantially smaller cross-sectional area than  
11 the area of either cavity so that pressurization of a first cavity results in deflection of  
12 a deflectable portion in communication with the second cavity.
- 13 68. The device of claim 63, wherein the cavities are pressurized using a gas from a high  
14 pressure reservoir.
- 15 69. The device of claim 68, wherein the gas is humidified.
- 16 70. The device of claim 63, wherein the cavities are pressurized at a pressure ranging  
17 from 1 – 200 psi.
- 18 71. The device of claim 63, wherein the cavities are pressurized at a pressure ranging  
19 from 1-30 psi.
- 20 72. The device of claim 63, wherein the cavities comprise an assembly of tubes that are  
21 blind at one or both ends, and wherein at least some of the tubes are connected to a  
22 high pressure reservoir.
- 23 73. The device of claim 63, wherein the cavities comprise an assembly of tubes that are  
24 blind at one or both ends, and wherein each of the tubes is connected to a high  
25 pressure reservoir.
- 26 74. The device of claim 63, wherein the cavities comprise an assembly of tubes that are  
27 blind at one or both ends, wherein at least one of the tubes is connected to a high

- 1           pressure reservoir, and wherein the remaining tubes are interconnected with at least  
2           one other tube.
- 3   75.    The device of claims 72, 73, or 74, wherein the connection to a high pressure  
4           reservoir is via a valve that controls pressurization of the tube.
- 5   76.    The device of claim 63, wherein the cavities comprise an assembly of tubes that are  
6           connected to a high pressure reservoir, and wherein at least some of the tubes are  
7           connected to the atmosphere or to a low pressure reservoir at lower pressure than that  
8           of the high pressure reservoir.
- 9   77.    The device of claim 63, wherein the cavities comprise an assembly of tubes that are  
10          connected to a high pressure reservoir, and wherein at least one of the tubes is  
11          connected to the atmosphere or to a low pressure reservoir at lower pressure than the  
12          high pressure reservoir, and wherein the remaining tubes are interconnected with at  
13          least one other tube.
- 14   78.    The device of claim 76 or 77, wherein the connection to the atmosphere or to a low  
15          pressure reservoir is via a valve that controls flow of gas through the tube.
- 16   79.    The device of claim 76 or 77, wherein the the cavities are connected at one end to a  
17          high pressure reservoir and at the other end to a valve which can be vented to the  
18          atmosphere or to a low pressure reservoir so that when a valve is closed, the  
19          corresponding cavity is pressurized, resulting in deflection, and when the valve is  
20          opened, gas flows through the cavity and the cavity is depressurized.
- 21   80.    The device of claim 63, wherein the cavities are located within the housing.
- 22   81.    The device of claim 63, wherein a deflectable portion separates a cavity from the  
23          interior of the chamber.
- 24   82.    The device of claim 63, wherein at least some of the cavities are connected to an  
25          actuation interface port.
- 26   83.    The device of claim 82, further comprising connecting means for connecting the  
27          actuation interface port to a high pressure reservoir or a low pressure reservoir.

- 1 84. The device of claim 82, further comprising an array of valves for controlling flow  
2 from the high pressure reservoir into the cavities or from the cavities to a low  
3 pressure reservoir or the atmosphere.
- 4 85. The device of claim 84, further comprising a manifold that interfaces the array of  
5 valves with the cavities.
- 6 86. The device of claim 1, wherein the chamber has at least one access port allowing  
7 introduction of fluid into the chamber or removal of fluid from the chamber.
- 8 87. The device of claim 1, wherein the chamber has at least two access ports allowing  
9 introduction of fluid into the chamber or removal of fluid from the chamber.
- 10 88. The device of claim 1, wherein the chamber has at least four access ports allowing  
11 introduction of fluid into the chamber or removal of fluid from the chamber.
- 12 89. The device of claim 1, further comprising a high pressure reservoir.
- 13 90. The device of claim 89, wherein the high pressure reservoir is filled with gas having  
14 a higher oxygen concentration than that in ambient air at standard temperature and  
15 pressure.
- 16 91. The device of claim 89, wherein the gas is humidified.
- 17 92. The device of claim 1, further comprising a low pressure reservoir.
- 18 93. The device of claim 1, further comprising a computer.
- 19 94. The device of claim 1, further comprising means for sensing a parameter selected  
20 from the group consisting of: pH, dissolved oxygen, optical density, substrate  
21 concentration, and product concentration.
- 22 95. The device of claim 94, wherein the sensing means comprises a fluorescence-based  
23 detector.
- 24 96. The device of claim 94, wherein the sensing means comprises a chemical detector.
- 25 97. The device of claim 94, wherein the sensing means is located within the chamber.



- 1 98. The device of claim 1, wherein the device comprises a plurality of chambers having  
2 selectively deflectable gas-permeable portions.
- 3 99. The device of claim 98, wherein each portion is deflectable by pressurizing a cavity  
4 in communication with the deflectable portion or by pressurizing a cavity in  
5 communication with a different deflectable portion.
- 6 100. The device of claim 99, wherein the cavities extend across multiple chambers so that  
7 pressurization of a single cavity results in deflection of a deflectable portion into  
8 each of the multiple chambers.
- 9 101. The device of claim 99, wherein the chambers and cavities comprise layers within an  
10 elastomeric block.
- 11 102. The device of claim 99, wherein the cavities comprise an assembly of tubes that are  
12 blind at one or both ends and that are connected either to a high pressure reservoir, a  
13 low pressure reservoir, to another tube, or to a combination of the foregoing.
- 14 103. A device comprising a set of tubes made at least in part of a gas-permeable material,  
15 wherein the tubes form portions of a wall of a chamber, and wherein the portions of  
16 the wall are selectively deflectable into the interior of the chamber.
- 17 104. A device comprising a set of tubes made at least in part of a gas-permeable material,  
18 wherein the tubes are separated from the interior of a chamber by a layer of gas-  
19 permeable material that forms a wall of the chamber, wherein the tubes are  
20 selectively pressurizable, and wherein pressurization of the tubes causes portions of  
21 the wall to deflect into the interior of the chamber.
- 22 105. A method of achieving mixing and gas exchange of a volume of liquid comprising  
23 the steps of:  
24 (i) introducing a liquid into the chamber of the device of claim 1; and  
25 (ii) actuating the device so as to repetitively deflect the deflectable gas-  
26 permeable portions into the chamber.
- 27 106. A method of achieving mixing and gas exchange in a volume of liquid comprising  
28 the steps of:

- 1 (i) introducing the liquid into the chamber of the device of claim 63; and  
2 (ii) actuating the device so as to repetitively deflect the deflectable gas-  
3 permeable portions into the chamber, wherein deflection is accomplished by  
4 pressurizing the cavities.
- 5 107. The method of claim 105 or 106, wherein the gas-permeable portions are deflected in  
6 a sequence that produces peristaltic action.
- 7 108. The method of claim 105 or 106, wherein mixing of two initially unmixed liquids is  
8 essentially complete within 1 minute of actuation.
- 9 109. The method of claim 105 or 106, wherein mixing of two initially unmixed liquids is  
10 essentially complete within about 10 seconds of actuation.
- 11 110. A method of culturing cells comprising:  
12 (i) introducing cells and a liquid cell culture medium into the chamber of the  
13 device of claim 1; and  
14 (ii) actuating the device so as to repetitively deflect the deflectable gas-  
15 permeable portions into the chamber.
- 16 111. A method of culturing cells comprising the steps of:  
17 (i) introducing cells and a liquid cell culture medium into the chamber of the  
18 device of claim 63; and  
19 (ii) actuating the device so as to repetitively deflect the deflectable gas-  
20 permeable portions into the chamber, wherein deflection is accomplished by  
21 pressurizing the cavities.
- 22 112. The method of claim 110 or 111, wherein the gas-permeable portions are deflected in  
23 a repetitive sequence that produces peristaltic action.
- 24 113. A method of making a device for fluid mixing and gas exchange comprising steps of:  
25 (i) fabricating a first layer defining a chamber;  
26 (ii) fabricating a second layer defining a plurality of cavities;  
27 (iii) fabricating a third layer comprising a gas-permeable material; and  
28 (iv) bonding the layers so that the third layer is interposed between the first  
29 and second layers so as to separate the chamber from the cavities and comprises

- 1 portions that are selectively deflectable into the chamber upon pressurization of the  
2 cavities.
- 3 114. The method of claim 113, wherein the third layer is fabricated as part of the first  
4 layer and forms a wall of the chamber.
- 5 115. The method of claim 113, wherein the third layer is fabricated as part of the second  
6 layer and forms a wall of the cavities.
- 7 116. The method of claim 113, wherein the first layer defines a plurality of chambers and  
8 wherein following step (iv) the cavities extend across the plurality of chambers.
- 9 117. The method of claim 113, wherein the cavities comprise an assembly of blind-ended  
10 tubes.
- 11 118. The method of claim 113, wherein the layers are fabricated from a gas-permeable  
12 elastomeric material.
- 13 119. The method of claim 113, wherein the first layer, the second layer, or both are  
14 fabricated from a material selected from the group consisting of: glass, plastic, or  
15 metal.
- 16 120. The method of claim 113, wherein the third layer comprises a PDMS membrane.
- 17 121. The method of claim 113, further comprising the step of interfacing the device to  
18 means for pressurizing the cavities.
- 19 122. The method of claim 121, wherein the means for pressurizing the cavities comprises  
20 an array of valves.
- 21 123. The method of claim 121, wherein the means for pressurizing the cavities comprises  
22 a high pressure reservoir.
- 23 124. The method of claim 113, wherein the chamber is macroscopic.

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